

accumulations of lymphoid tumor cells, small and uniform in size same as found in the lung. The cells were infiltrated to the surrounding tissue and around the glomeruli. Deposit materials of blue crystal in the tube lumen were found in several areas. Some kidney tubules were degenerated to necrotic. Necrotic areas in some parts of spleen were also noticed. Most lymph nodes were congested. There were no histopathological lesion in the pancreas, ovary and uterus.

Based on all these findings mention above, we diagnosed that the tiger was suffered from lymphoma and parasites infection (Filariosis) probably due to larvae migrant.

[Session III] #10

The Occurrence of Neoplastic Diseases in Long Evans Rats of a 2-yr Feeding Study

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In Taiwan, toxicologic pathology task work in safety assessment for preclinical trial drug safety investigation or in toxicity study/ carcinogenicity bioassay for chemical and environmental issues is rather young. It has been a little bit more than a decade since the inception of this field. The current demanding

of safety assessment is primarily due to recent growth of a demand for research and development (R&D) in herbal medicinal products and health foods primarily that led to start business and founding of contract research organizations (CRO) on the island. The safety assessment trials, however, are primarily stagnated in acute and short-term subchronic toxicity study under current trend of business. Studies involving medicinal, agricultural and environmental chemicals are fairly few but are coming slowly. In 2002, the federal sector in the Ministry of Economic Affairs (MOEA) launched a campaign to encourage R&D interesting for improving and strengthening capability in small and medium-sized industrials. One big concern is CRO capability in performing chronic toxicity/ carcinogenicity preclinical trial that needs long term performs up to 2 years under barrier system with SPF lab animals per Standard Operating Procedure (SOP). This is also a step toward GLP level and greater credibility. The work is big Greenseasons Biotech Co., a private and one of the two major CROs on Taiwan accepted and performed this challenge by running a 2-year study with Long Evans (LE) and Wistar(WI) rats. The project was partial financially supported by the MOAE. The present report presents the occurrence of neoplasm in Long Evans rats with the 2-yr exposure period.

The study was conducted in 190 LE male and female LE rats starting at the age of 8 weeks. Ten rats in each sex were fed for 28-, 90-, 180-days, or 1-yr on exposure (yoe), 15 each for 1.5-yr, and 40 each for 2-yr. A total of 56 male and female rats

were found dead (FD) or killed *in extremis* (KE) at their different exposure. These 56 terminated prematurely were 3 males and 5 females at the 1.5-yoe, and 26 males and 22 females at 2-yoe. The survival rate for 1.5-year study was 80% (12/15) in males and 66% (10/15) in females, and for 2-year study was 35% (14/40) in males and 55% (18/40) in females.

Pathology evaluation revealed a total of a total of 33 kinds primary tumors were observed in male and female LE rats. These tumors were 1) Schwannoma (heart), 2) hemangioma (heart), 3) hepatocellular adenoma /carcinoma, 4) lymphoma (Peyer's patches, mesenteric lymph node, multicentric), 5) islet cell adenoma/carcinoma, 6) acinar cell adenoma (pancreas), 7) malignant hibernoma (kidney), 8) renal tubule adenoma, 9) lipoma (kidney), 10) bladder papiloma, mediastinum), 11) uterine adenocarcinoma, 12) endometrial stromal polyp/sarcoma, 13) uterine leiomyosarcoma, 14) uterine squamous cell carcinoma, 15) Leydig cell adenoma, 16) pheochromocytoma, 17) pheochromocytoma complex, 18) adrenal cortical adenoma, 19) thyroid follicular adenoma/ carcinoma, 20) C-cell adenoma, 21) pituitary pars distalis adenoma, 22) hemangiosarcoma (spleen), 23) large granular lymphocytic lymphoma (spleen), 24) granulocytic leukemia, 25) angiosarcoma (mesenteric lymph node), 26) thymic adenoma, 27) glioma/mixed glioma, 28) granular cell tumor (brain), 29) osteosarcoma, 30) fibroma/fibrosarcoma (skin, mammary), 31) mammary adenoma, 32) mammary fibroadenoma and 33) melanoma (ear pinna). Of these 33 kinds, 28 types were observed in males and 22 types in females of the entire

LE rat population in this study. For further databases in detail of these 33 kinds, 5 kinds were observed in the 1.5 yoe rats. Of that 4 of the 5 kinds in the males and also other 4 of the 5 in the females and 28 kinds were observed in males and 22 types in females of the 2-yr exposure. One-granulocytic leukemia, of the 5 neoplasms detected in the 1.5-yoe rats, was not observed in the 2.0-yoe rats. These occurring in the male and female LE rats at 1.5-y and 2-y exposure are summarized in Table 1.

Of these 33 kinds primarily neoplastic diseases, a total of 21 male and female rats died from neoplastic diseases with 3 males and 2 females in the 1.5-yoe and 2 males and 7 females in the 2-yoe study. A summary of these are presented in Table 2.

Other information regarding neoplastic diseases occurring in these LE rats will be further presented.

[Session III] #11

Antioxidant Related Protein, Senescence Marker Protein-30 (SMP30), has an Inhibitory Effect on the Hepatic Fibrogenesis of Smad3-Mutant Mice

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